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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
YU, MISOOK

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/26/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/903,023	WANDS ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,39-47 and 49-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *57* is/are allowed.

6)☒ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *1-9, 39-47, 49-56, 58-61* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-9, 39-47, and 49-61 are pending and Claims 1-9, 39-47, and 49-61 are examined on merits.

Claim Rejections - 35 USC § 112

Rejection of claims 1-8, 39, 40, 43, 45, 46, 51, and 52 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps **is withdrawn** because applicant added the previously missing determination step in the instant claims.

Rejection of claim 41, 42, 44, 47-50, 53, and 54 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps **is withdrawn** because applicant added the previously missing determination step.

Rejection of claims 1, 9, and 41 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention because the claims recite "under conditions sufficient to form an antigen-antibody complex" **is withdrawn** because applicant argument is persuasive.

Rejection of claims 9 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention because the claim recite "normal control level" **is moot** because the claim no longer recite the limitation.

Claims 1-9, and 39, 40, 43, 46, 51, and 52 **remain rejected** and the new claims 58, and 59 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to **use** the invention. Applicant argues that an increase in HAAH level both in bodily fluid samples and in tissue samples correlate with a diagnosis of malignancy. First, applicant's argument with higher expression in tissue samples is not commensurate in scope with the instant claims because the instant claims are drawn to method of using

bodily fluid, not tissue samples. As stated in the previous office action (note the paragraph bridging pages 3 and 4), previous studies (see C19, C35, C38 of the IDS, all of these references more than one year before the effective filing date of the instant application) as well as the instant specification have established using previously known monoclonal antibody FB50 that high-level HAAH expression in numerous malignant ***tissue samples*** exists. However, the high-level HAAH expression were detected in the specimen obtained from surgical resection of tumor (pages 36, lines 6-23), not from the source recited in the limitation of the instant claims. Contrary to applicant's argument the Office did not reject the instant claims because no correlation exists between higher expression of HAAH (as compared to normal control) in tissue samples to presence of tumor. As for applicant's argument that an increase in HAAH level in bodily fluid correlates with a diagnosis of malignancy is not convincing because the data in Table 1 at page 2 of Dr. Lebowitz's declaration filed 8-13-2002 shows that HAAH is positive in bodily fluid samples of more than 6 percent of normal non-cancerous control while HAAH is negative in bodily fluid samples of 30 percent of breast cancer patients. Considering the state of art unpredictability of using a biomarker in bodily fluid for cancer diagnostic marker as demonstrated by Weg-Remers et al and Teillac et al (cited in the previous Office action), limited teaching of the specification, and unpredictability of cancer detection using HAAH detected in bodily fluid in Dr. Lebowitz's declaration, it is maintained that one skilled in the art would have reasons to question the efficacy of the claimed method for cancer diagnosis and requires undue experimentation involving analysis of a large amount clinical samples.

Rejection of claims 41, 42, 44, 47, 49, 50, 53, and 54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention **is withdrawn** because the claims are now drawn to method of cancer diagnosis but detecting higher expression of HAAH as compared to detection of its expression.

Claim Rejections - 35 USC § 102

Rejection of claims rejected under 35 U.S.C. 102(b) as being anticipated by Lavaissiere et al (C19 of the IDS) **is withdrawn** because the base claim, claim 41 is now drawn to method of CNS cancer diagnosis by detecting HAAH over-expression and the prior art does not specifically discloses expression in CNS cancers.

NEW GROUNDS OF REJECTION

Claim Objections

Claim 47 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The cancer in the instant claim is not CNS cancer.

Claim Rejections - 35 USC § 112

Claims 55 and 56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims recite specific monoclonal antibodies produced by specific cell lines.

It is apparent that the recited antibodies are required to practice the claimed invention, because they are specifically required in the claims. As required elements they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the cell lines producing the specific monoclonal antibodies in claim 55. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining the antibodies produced by the cell lines of claim 55, and they do not appear to be readily available material. Deposit of the cell lines would satisfy the enablement requirements of 35 U.S.C. 112.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Cl im Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 41, 42, 44, 53, 54, 60, and 61 are rejected under 35 U.S.C. **102(a)** as being anticipated by De la Monte et al (IDS 34, 01-1999, Modern Pathology 12:170A). All cancelled

The claims are interpreted as drawn to CNS cancer diagnosis by detecting overexpression (**quantity of protein concentration higher instead of binary test of either presence or absence for determination step)** of HAAH in bodily tissue by immunohistochemistry. De la Monte et al teach HAAH protein overexpression in CNS cancers, thus anticipating instant claims. It is noted that there is no difference in data between the instant application and the prior art, thus the prior art anticipates instant claims.

Claim 45 rejected under 35 U.S.C. **102(b)** as being anticipated by Lavaissiere et al (IDS C19, 1996, J. Clin. Invest. 98, pages 1313-1323).

The claim is drawn interpreted as drawn to hepatocellular cancer diagnosis by detecting overexpression of HAAH in bodily tissue by immunohistochemistry. Lavaissiere et teach overexpression of HAAH in hepatocellular carcinoma. There is no difference in disclosure between the instant application and Lavaissiere et al, thus Lavaissiere et al anticipates instant claim.

maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over De la Monte et al (cited supra) as applied to claims 41, 42, 44, 60, 61 above, and further in view of Huse (1992, Antibody Engineering, Borrebaeck C ed., page 103-107 only). cancelled

The primary reference teaches CNS cancer diagnosis by detecting HAAH overexpression by antigen and antibody immunostaining but does not specially mention that a single chain Fv fragment antibody against HAAH. However, Huse teaches making a single chain antibody from an antibody specific for a known antigen is a routine procedure in the art and one in ordinary skill knows generating a single chain Fv antibody against a useful antigen is cost-effective because it takes less time to purify the antibody.

Claim 50 is rejected under 35 U.S.C. 103(a) as being unpatentable over De la Monte et al (cited supra) as applied to claims 41, 42, 44, 60, 61 above, and further in view of Huse (1992, Antibody Engineering, Borrebaeck C ed., page 103-107 only) further in view of Lavaissiere et al (cited supra) cancelled

Lavaissiere et al teach FB-50 antibody, therefore detection of the CNS cancer using a single chain FB-50 Fv antibody is another variation of the primary reference that one in ordinary skill could do with reasonable expectation of success.

Allowable Subject Matter

Although either Lavaissiere et al (cited supra) or De la Monte et al teach overexpression of HAAH in many human, none of the references teach or suggests its overexpression in pancreatic cancer. The Office is well aware of that fact that both liver cancer and pancreatic cancer are from same origin, i.e., endodermal origin. However, the Office position is that it is difficulty to predict for a biomarker for liver cancer could be used as a biomarker for pancreatic cancer unless experimental data prove otherwise. Dr. Lebowitz declaration at page 3 says HAAH is overexpressed in pancreatic cancer as compared to normal noncancerous control, therefore claim 57 is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Misook Yu whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Misook Yu
March 22, 2003